

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
17 February 2005 (17.02.2005)

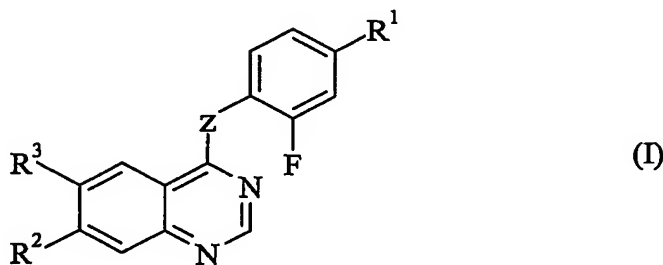
PCT

(10) International Publication Number  
**WO 2005/013998 A1**

- (51) International Patent Classification<sup>7</sup>: **A61K 31/517**,  
C07D 401/12, 403/12, A61P 9/00
- (21) International Application Number:  
PCT/GB2004/003393
- (22) International Filing Date: 5 August 2004 (05.08.2004)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:  
0318423.1 6 August 2003 (06.08.2003) GB
- (71) Applicant (for AE, AG, AL, AM, AT, AU, AZ, BA, BB, BE, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CY, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, SZ, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW only): **ASTRAZENECA AB** [SE/SE]; Sodertalje, SE-151 85 (SE).
- (71) Applicant (for MG only): **ASTRAZENECA UK LIMITED** [GB/GB]; 15 Stanhope Gate, London, Greater London W1K 1LN (GB).
- (72) Inventor; and  
(75) Inventor/Applicant (for US only): **HENNEQUIN, Laurent, Francois, Andre** [FR/FR]; AstraZeneca Pharma, Z.I. la Pompelle, BP 1050, F-51689 Reims (FR).
- (74) Agent: **ASTRAZENECA**; Global Intellectual Property, SE-151 85 Sodertalje (SE).
- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,

[Continued on next page]

(54) Title: QUINAZOLINE DERIVATIVES AS INHIBITORS OF VEGF RECEPTOR TYROSINE KINASES



(57) Abstract: The present invention relates to compounds of the Formula (I): wherein Z is -NH-, -O- or -S-; R<sup>1</sup> represents bromo or chloro; R<sup>3</sup> represents C<sub>1-3</sub> alkoxy or hydrogen; R<sup>2</sup> is selected from one of the following three groups: (i) Q<sup>1</sup>X<sup>1</sup> - wherein X<sup>1</sup> and Q<sup>1</sup> are as defined herein; (ii) Q<sup>15</sup>W<sup>3</sup> - wherein Q<sup>15</sup> and W<sup>3</sup> are as defined herein; and (iii) Q<sup>21</sup>W<sup>4</sup>C<sub>1-3</sub>alkylX<sup>1</sup> wherein X<sup>1</sup>, W<sup>4</sup> and Q<sup>21</sup> are as defined herein; and salts thereof; their use in the manufacture of a medicament for use in the production of an antiangiogenic and/or vascular permeability reducing effect in warm blooded animals; processes for the preparation of such compounds; pharmaceutical compositions containing a compound of formula (I) or a pharmaceutically acceptable salt thereof and methods of treating disease states involving angiogenesis by administering a compound of formula (I) or a pharmaceutically acceptable salt thereof. The compounds of formula (I) inhibit the effects of VEGF, a property of value in the treatment of a number of disease states including cancer and rheumatoid arthritis.

WO 2005/013998 A1



SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

**Published:**

— *with international search report*